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Case Report

Pulmonary thromboembolism and thrombolytic treatment in total knee arthroplasty: A case report

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Abstract
Pulmonary thromboembolism (PTE) is a fatal complication of total knee arthroplasty (TKA). Thrombolytic treatment is of critical importance in PTE treatment. In patients not administered thromboprophylaxis in TKA operations, deep vein thrombosis (DVT) has been reported at the rate of 50-70%, PTE at 5%, and fatal PTE at 1-4%. In this study, we present a case who developed PTE after TKA surgery. Thrombolytic therapy, which is an absolute contraindication in the treatment of massive PTE after major orthopedic surgery, can become a relative contraindication in life-threatening situations, and early diagnosis and treatment in a short time can be life-saving without causing major bleeding.

Keywords
Pulmonary Thromboembolism, Thrombolytic Treatment, Total Knee Arthroplasty, Ultrasonography, Echocardiography

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Introduction

PTE is the condition forming as a result of a thrombus blocking the pulmonary artery and branches, which usually forms in the deep veins of the lower extremities and occasionally in other veins throughout the body (upper extremities, abdomen). PTE can occur in three forms; first as a non-massive form with normal systemic blood pressure and right ventricle functions, second as a submassive form in which blood pressure is normal but right ventricular dysfunction findings (right ventricular dilatation, moderate and severe hypoxia, paradoxical movement in the septal wall and deviation to the left) on echocardiography, and third as a massive form, which is the most severe with hypotension, right ventricle dysfunction, shock, and cardiopulmonary arrest (Arseven O, Bingöl Z, Çöplü L, Erol S, Oğuzülgen İK, Okumuş NG, et al. Arseven O, editor. Pulmoner Tromboembolizm Tanı ve Tedavi Uzlaşı Raporu/ Pulmonary Thromboembolism Diagnosis and Treatment Consensus Report. Türk Toraks Derneği/ Turkish Thoracic Society. 2021. p. 1-124). In patients not administered thromboprophylaxis in TKA operations, deep vein thrombosis (DVT) has been reported at the rate of 50-70%, PTE at 5%, and fatal PTE at 1-4%. In patients applied with DVT prophylaxis, DVT has been reported at the rate of 0.9-5%, PTE at 0.27-1.1%, and fatal PTE at 0.1-0.5%. The risk of PTE is significantly higher following simultaneous bilateral TKA than following single unilateral TKA [2-4].

There are several risk factors causing PTE, the most important of which are major orthopaedic surgical interventions. Dyspnea, tachypnea, tachycardia, persistent hypotension (systolic blood pressure ≤90 mmHg or arterial blood pressure ≥40mmHg compared to the basal value within 15 mins under observation), pleuritic lateral chest pain, cough, hemoptysis, cyanosis, anxiety, a feeling of substernal pressure, mental confusion, and syncope may be seen in PTE cases. It has been stated that ≥50% of the pulmonary vessel bed is obstructed in massive PTE [1]. The most important step in diagnosis is suspicion of PTE. Patients with suspected PTE must be rapidly evaluated and for diagnosis, examinations must be made first of D-dimer, lower extremity compression ultrasonography, echocardiography, and multidetector computed tomography (CT) angiography .

In the treatment of PTE, general supportive treatment is applied together with anticoagulant treatment, thrombolytic treatment, embolectomy performed with surgery and percutaneous catheter techniques, and vena cava inferior filter [2, 3]. Thrombolytic drugs, which provide active dissolution of the thrombus by converting plasminogen to plasmin, are the drugs first administered in PTE treatment. Currently, the most commonly used thrombolytic drugs are recombinant human tissue-type plasminogen activator (alteplase), streptokinase, and urokinase. The main indication for thrombolytic treatment is massive PTE in which persistent hypotension develops without another associated cause such as newly emerging arrhythmia, hypovolemia, and cardiogenic shock, and/or sepsis. It has been stated that when thrombolytic treatment is administered within 48 hours, it is more effective [2].

Our aim in presenting this case is to show that thrombolytic therapy, which is an absolute contraindication in the treatment of massive PTE after major orthopedic surgery, can become a relative contraindication in life-threatening situations, and that early diagnosis and treatment in a short time can be life-saving without causing major bleeding.

Case Report

The patient was a 67-year-old female (height 1.58 cm and weight 87 kg), with a history of type 2 diabetes mellitus and hypertension. No pathology was determined in the routine preoperative tests. Bilateral TKA was performed under spinal anesthesia, using a tourniquet, with a parapatellar medial incision to both knees. At 6 hours postoperatively enoxaparin sodium 4000 IU (Clexane 0.4ml) was administered subcutaneously as thromboprophylaxis. On the postoperative first day, dyspnea, tachypnea (34/min), tachycardia (132/min), and hypotension (70/30 mmHg) developed suddenly. The patient seemed distant but was conscious, and oxygen saturation was (SpO2) 60%.

As the preoperative tests of the patient were normal, the above-mentioned clinical findings were present, and major orthopaedic surgery had been performed, massive PTE was the first pathology that came to mind. With rapid coordination of the cardiology and thoracic departments, the patient was admitted to the surgical Intensive Care Unit (ICU). Supportive treatment was started immediately (monitorisation, and oxygen was administered with mask [3-4lt/min]). Until the diagnosis was confirmed, 0.8ml enoxaparin sodium 8000 IU (Clexan 0.8ml) was administered subcutaneously. In the patient monitorisation, there were findings of right ventricle failure on electrocardiography (ECG) (Figure 1). In the arterial blood gases, pH was determined as 7.32, PCO2 24.6 mmHg, PO2 56.8 mmHg, and acid-base status cBase(Ecf)c -12.6 mmol/L. In bedside echocardiography, right ventricle diameter was 36 mm (normal <25mm), pulmonary artery pressure was 70 mmHg (normal <30mmHg), and there were moderate-advanced tricuspid failure and widespread thrombus in the right ventricle. The recombinant human tissue-type plasminogen activator (rt-PA, alteplase = Actilyse 50 mg, Boehringer Ingelheim, Germany) 100 mg was administered as a 10 mg intravenous bolus within 1-2 mins, and the remaining 90 mg as an intravenous infusion within 2 hours.

On the bedside transthoracic echocardiography taken at the end of two hours, the thrombus was observed to have completely

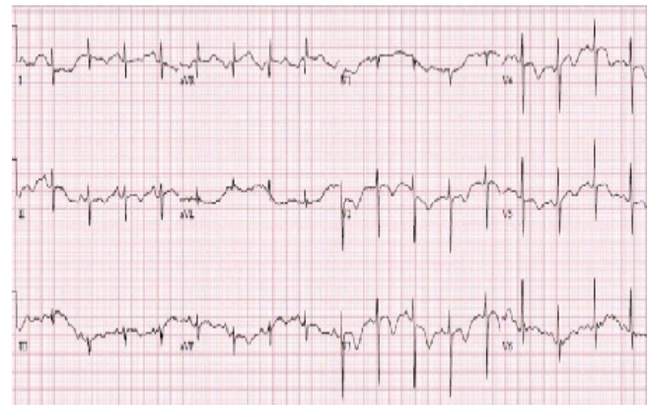

Figure 1. Abnormal ECG findings in the patient diagnosed with PTE (Sinus tachycardia, left axis deviation, T wave abnormality, R wave progression)

disappeared, the ventricle diameter was close to normal (28mm), pulmonary artery pressure decreased (32 mmHg), tricuspid failure regressed to a mild level, blood pressure was measured as 110/60 mmHg, pulse 105/min, and SpO2 94%. At three hours after the thrombolytic drug treatment, arterial blood gas values were measured as pH 7.42, PCO2 33.2 mmHg, PO2 99.1 mmHg, and acid-base status cBase(Ecf)c -2.6 mmol/L. On the second day (12 hrs after thrombolytic drug administration) enoxaparin sodium 2 x 0.8 ml was started. Multidetector-CT angiography, which could not be made earlier because the hemodynamics of the patient were not suitable, was performed on day 3 together with peripheral venous CT angiography. No thrombus was observed in the pulmonary artery - branches, and in the deep venous system of both lower extremities. After compression bandages were applied to the extremities and follow-up of bleeding, the Hemovac drain was removed 48 hours later, and venous compression ultrasonography taken on day three was normal in both lower extremities.

No major bleeding associated with the thrombolytic drugs was observed in the patient. There was a total of 300 cc blood from the Hemvac drain from the right knee and 350 cc from the left knee. No significant bleeding was determined at the operation site. Some ecchymosis was determined only in the knee region and the region of bleeding. Throughout the treatment, four units of erythrocyte suspension were administered. After five days of follow-up in ICU, blood pressure was measured as 119/61 mmHg, pulse 92/min, SpO2 95% (without mask), respiratory count 20/min, so the patient was transferred to the chest diseases ward in a good condition. Following removal of the sutures on day 13, 5 mg of oral warfarin was added to the 2 x 0.8ml enoxaparin treatment. When the International Normalized Ratio (INR) values reached 2-3, the enoxaparin was terminated, warfarin was continued at a dose of 3 mg, and the patient was discharged.

At the 3-month follow-up examination in the chest diseases department, ventilation/perfusion scintigraphy and venous compression ultrasonography in both lower extremities were normal, and therefore warfarin was terminated and ticlopidine (ticlocard 250 mg) was administered. Now in the 8th postoperative year, there has been no new DVT or PTE attack in this patient. The Knee Society arthroplasty evaluation knee score was determined to be 92 (excellent) and the knee function score was 90 (excellent). Written informed consent was obtained from the patient for the publication of this study.

Discussion

Massive PTE is a fatal complication of TKA, with reported mortality rates of 2-8% in cases with treated PTE and 25-30% in untreated cases. Difficulty in rapid and early diagnosis, the risk of bleeding from anticoagulants given before diagnosis, the time taken for diagnostic tests, and the bleeding complications of the thrombolytic drugs recommended in treatment, constitute a problem in PTE. It has been stated that >50% of the deaths of PTE patients occur in the first hour [1]. Therefore, action must be taken very rapidly. In the current case, the time from clinical suspicion to starting thrombolytic treatment was one hour.

To be able to cope with these difficulties, reduce the risks, gain time for diagnosis, and reach a correct diagnosis without stress in patients who have undergone a major orthopaedic operation such as TKA, PTE should first come to mind when there is sudden development of dyspnea, tachypnea, tachycardia, mental confusion, lateral chest pain, cyanosis, persistent hypotension, and shock, and the patient must be admitted immediately to surgical ICU, life support must be provided, and if there is a delay in diagnosis and no contra-indications, anticoagulant treatment should be started immediately [1]. If the hemodynamic status of the patient is not suitable and/or there is no opportunity to apply multidetector-CT angiography, bedside transthoracic echocardiography should be performed first. As the current patient did not have stable hemodynamics, bedside transthoracic echocardiography was performed first and thrombus was determined in the right ventricle.

The presence of right ventricle dysfunction, thrombus in the right atrium and/or right ventricle, and pulmonary hypertension on echocardiography is sufficient for a diagnosis of massive PTE. Echocardiography is the first procedure to be applied in patients with suspected PTE when multidetector-CT angiography cannot be taken [3]. When there is suspicion of PTE, if the patient is hemodynamically stable and multidetector-CT angiography can be taken, this method should be performed [4]. Bedside lower extremity compression ultrasonography should also be performed in patients with suspected PTE, if available. The presence of a thrombus on ultrasonography supports the diagnosis of PTE [5]. Despite DVT seen together with PTE at the rate of 16.9%-56.4%, it generally has an asymptomatic course, and the first symptoms associated with PTE in patients may be dyspnea, tachypnea, and tachycardia [4.5]. In the current patient, thrombus was determined on echocardiography, and additional tests of D-dimer, serum cardiac troponins, and natriuretic peptides were not considered to be necessary for the diagnosis of massive PTE.

If there is no contra-indication, thrombolytic drugs are the treatment approach first selected in the treatment of massive PTE [2]. Of the thrombolytic drugs available, recombinant human tissue-type plasminogen activator has the advantages of a shorter plasma half-life (2-6 mins) and duration of application (two hours) than other thrombolytic drugs. It is not necessary to terminate it before starting anticoagulants, and there are few bleeding complications despite the rapid administration [6]. The most significant side-effect of thrombolytic drugs is that they increase the risk of bleeding. These bleedings may be in the form of minor bleeding such as bleeding in the region of intramuscular injection or major bleeding such as intracranial, gastrointestinal, and retroperitoneal bleeding. The rate of major bleeding of thrombolytic drugs has been stated to be 3-21.7%, and intracranial or fatal hemorrhage as 1.8-3% [2,6]. Therefore, they must be used with great attention paid to the benefit-harm relationship. There are absolute and relative contra-indications to thrombolytic treatment. Having undergone major orthopedic surgery within the last 3 weeks is one of the absolute contra-indications [7]. However, as in the current patient, it may become a relative contra-indication in life-threatening massive PTE cases. As the hemodynamics of the current patient were not stable, and with the thought that the life of the patient could be lost with the preparation time for emergency surgery or percutaneous catheter embolectomy, thrombolytic treatment

was considered correct and was therefore administered. No major bleeding occurred in this patient.

If thrombolytic drugs cannot be used in patients with massive PTE or if there is no response to treatment and conditions are suitable, these are indications for surgery or percutaneous catheter embolectomy [7]. However, it must not be forgotten that these procedures take time and carry risks. In patients with massive PTE with contra-indications for anticoagulant treatment, those who develop complications under treatment, or develop recurrence under anticoagulant treatment, the vena cava inferior filter is one of the methods that can be used. However, although the vena cava inferior filter is an effective alternative treatment method, it is not currently frequently used because of complications [1].

Conclusion

With early diagnosis followed by rapid and correct treatment, massive PTE may not be fatal. Time is of vital importance in PTE cases. By providing appropriate conditions for these patients, and taking precautions against bleeding complications, thrombolytic treatment can be applied and be life-saving.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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